# SOME ASPECTS OF THE RELATIONSHIP BETWEEN MOTHER AND CHILD

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I MUST, at once, say what a pleasure it is to see so many old friends again, and I must thank most warmly those who have put me into my present privileged position. Effectively to recapture the past is beyond most of us. The attempt by an individual to do so, however, can be pleasurable and may be salutary or even poignant. But be the reaction as it may, the evocation of old and partly forgotten experience is sometimes a pious duty—as it is for me on this occasion.

I joined the medical school here, in the company of several who are also present tonight, nearly thirty-five years ago. Since I left Belfast, after having been successively student, houseman at the Royal, and demonstrator of anatomy, a quarter of a century has elapsed. My memories of this medical school, therefore, which are very happy ones, go back a long way, encompass a considerable period, and, in some respects, are remarkably clear. If the occasion were opportune what tales I could relate, and not only of my fellow-undergraduates!

Unfortunately these memories, in the context of tonight's commemoration, do not go back far enough for me to give you a first-hand and coherent account of Robert Campbell. His name was held in the highest regard by our clinical teachers, who had been his colleagues and pupils. And to this vicarious knowledge of him I can add one piece of direct evidence on the manner of man he was. My father-in-law, who knew him well, used to tell of sitting beside him in a tram. Robert Campbell suddenly emerged from a small volume in which he was immersed to exclaim—"There's the best definition of life I have met!" The book was *Measure for Measure*; the line indicated was "*This sensible warm motion*"—from Claudio's moving speech in the first scene of the third act. Such an anecdote, trivial though it may seem, surely limns the character! He was a successful, and busy, surgeon who read Shakespeare in a tram-car, and read him with critical and sensitive attention. Of Robert Campbell's high standing in his profession you will have been told in previous orations, made by those better able, by far, to judge on such a matter than can I. Nevertheless, I must record that I have heard high praise of him, and of his work—as a pioneer in aseptic surgery, as first in the diagnosis of the obstructed appendix, as brilliant innovator in the repair of infantile herniæ. And I have heard this praise in regions where it was not underwritten by local patriotism. Robert Campbell was one of that distinguished group of Belfastmen who put the Queen's Medical Faculty on the

right road to its achieved, and present, high distinction. It is meet that he should be remembered here. I have been so long dissociated from active contact with clinical medicine that I feel myself peculiarly inappropriate as the commemorating orator. Nevertheless, it is possible that Robert Campbell would have been pleased that, like him, I was once a demonstrator in anatomy at Queen's. And as he had such a deep interest in the surgery of childhood it is even possible that he would have been interested in, at least, the subject I am committed to discussing.

None of you will expect from me a complete exposition of the relationship between mother and child. Such an exposition would, patently, be far beyond my competence. I am an anatomist, by trade and, indeed, by inclination. What I shall have to say will, therefore, relate primarily to structure, though, I hope, in the idiom of contemporary anatomy. I am sure you all must know that the climate of opinion in anatomy has undergone a revolutionary change in our lifetimes, and that it is now fully intercalated into the advancing front of contemporary biology. So if, from time to time, I leave the details of structure to consider their general implications, I shall not be exceeding what modern anatomists consider to be their duty.

For many years, both alone and in collaboration, I have had a continuing interest in the mammalian placenta. This most remarkable transient organ is, of course, the *sine qua non* in the fœtal-maternal relationship. Considering its basic importance, it is surprising how ignorant we remain about many fundamentally important aspects of its structure and function. I shall, perforce, have to restrict myself now to the human placenta, and, indeed, to certain particular aspects of it to which I have been able to give direct attention.

But, firstly, may I briefly orientate you on the basic structure and relations of the placenta (Pl. I, Figs. 1 and 2). Such an orientation requires a summary account of its origin for it is by knowing how structures arise that we can understand how they come to acquire the features they possess. The human zygote enters the uterine cavity as a blastocyst and, as the classical investigations of Hertig and Rock (1956, for summary) have shown, implants there during the seventh day after ovulation. At this time the endometrium is in the luteal phase of the uterine cycle. The uterus has been 'primed' for the reception of the blastocyst. Its lining is markedly thickened and its glands are much enlarged, tortuous, and full of secretion. The exact nature of the glandular secretion has yet to be determined, but we know that it contains lipids, protein (especially muco-protein) and glycogen. It possibly also possesses some lyzozyme-like quality which renders it bacteriostatic. There are a very large number of the endometrial glands, according to my own computations, not fewer than 15,000 of them. Their secretion presumably supplies an optimum background for the unimplanted blastocyst when it is lying free in the uterine lumen. The blastocyst becomes attached between the mouths of several of these active glands and rapidly makes its way through the mucosal epithelium so that soon, by the eleventh or twelfth post-ovulational day, it is completely implanted in the maternal tissues. The mechanism by which such interstitial implantation is effected is not well understood. In particular the precise rôles of egg and

endometrium in the process are unknown. The implanting blastocyst wall, or trophoblast, may produce a cytolytic enzyme which is responsible for the epithelial erosion at the point of contact, though there is no direct evidence available to establish this probability. From animal experiments, it is known that the uterine mucosa can embed inert objects. Every ectopic gestation demonstrates that implantation can take place other than in the uterus. To assign quite separate rôles to the conceptus and to the maternal tissues in the process is probably an over-simplification, for it is a mutual and remarkably tolerant relationship which is established. And to this tolerance I should like, for a moment, to direct your attention.

A fact of basic significance in the maternal-fœtal relationship is that (apart from animal strains so inbred that all their members are essentially homozygous) the genetic structure of mother and offspring is different. This, of course, is the reason why, in post-natal life, a skin graft from one to the other, in either direction, will not "take." Such a graft, like most other homografts, induces a reaction in the host whereby its immunological, anti-foreign protein resources are mobilised. Consequently, after a brief interval, the graft will be destroyed. The work of Medawar (1958) has shown that soluble antibodies are unlikely to be primarily concerned in effecting this destruction. Rather it is cells of the host's reticulo-endothelial system which are sensitized by the presence of products of the graft. Such sensitized cells are discharged into the blood stream and pass with it to the site of the graft and, once there, proceed to cast off the alien cells. Certain tissues, however, notably the cornea, cartilage, and the fibrous framework of arteries, can be successfully grafted. Whether this lack of susceptibility on the part of these privileged tissues is due to the absence in them of a vascular supply (as seems most likely); or to insulation and protection by the muco-polysaccharide of their matrices; or to absence of, or absence of liberation of, antigen is not altogether clear, and need not, here, be explored further. The point that must be made is that neither in the early stages, nor, indeed, at any stage in pregnancy, does the trophoblast of the placenta appear to behave as a sensitive or sensitizing homograft. That it is, in fact, a homograft there can be no doubt. Moreover the trophoblast is in most intimate contact, indeed, in direct contact, with the maternal blood in the intervillous space. Separated portions of it may come to lie in the depths of the endometrium, well away from the placental site and even in the myometrium (Pl. II, Figs. 3 and 4), yet I have never seen such trophoblast to induce such a reaction in the maternal tissues as is to be expected from its genetic structure. Even more curious, though the phenomenon is well established, small fragments, the so-called syncytial sprouts, of the trophoblast are continuously being discharged into the maternal circulation. They pass to the mother's lungs (Schmorl, 1893; Park, 1958), just as do the more spectacular metastases of chorio-epithelioma, where, however, they seem to undergo cytolysis. I have seen such syncytial sprouts in sections through uterine veins remote from the placenta (Pl. II, Figs. 5, 6, and 7), and my friend, Dr. Lewis Thomas, of Bellevue Hospital in New York, informs me that he has found them in blood removed from uterine veins during hysterotomy or Cæsarian section.

The absence of a homograft reaction to trophoblast on the part of the maternal organism is the more remarkable in view of the well-known formation of maternal hæmolysing antibodies to fœtal blood when the latter possesses certain special antigenic properties. Moreover, the tissues of the fœtus itself do not, at least in the rabbit, appear to possess significant protection against maternal antibodies (Woodruff, 1958). The notion of the placenta as a homograft is recent, but I hazard the opinion that, progressively, much more will be heard of the problems such as concept poses. In particular, it is important to establish whether the absence of a homograft reaction by the maternal organism to the embryonic trophoblast is complete or not. If the absence of response is only relative and can vary in any way with the genotypes involved certain puzzling problems in gestation and fertility may receive their explanation.

Well, then, the blastocyst becomes implanted in a prepared endometrium and is not treated there as our knowledge of homografts would lead us to expect. But if there is no immunological reaction to the trophoblast there is a most obvious local mechanical effect of the presence of the conceptus. The uterine glands are pushed aside—elbowed out of the way, as it were—by the enlarging chorionic tissue. Many glands are eroded by the trophoblast, and their secretions come into direct contact with it. This erosion of the glands continues for a long period, certainly until the end of the second month of gestation. Moreover, owing to the breakdown of the distal parts of the glands, secretion from them comes into direct contact with the trophoblast and, indeed, can pass directly into the intervillous space (I.V.S.) or into gaps, between the trophoblastic cells, which communicate with it (Pl. II, Fig. 8). This space is formed by the confluence of lacunæ in the early trophoblast; it is, therefore, of fœtal origin and lined by the trophoblast.

Maternal vessels come to open into the I.V.S. It is the endometrial veins that first establish communication, at the eleventh or twelfth day; only at a distinctly later date can the terminations of the coiling (spiral) arteries be found to discharge into the space. Initially, therefore, the maternal blood supply to the I.V.S. is in the nature of a venous ebb and flow. Not until the arterial connections are established can an actual circulation of maternal blood in the space occur. Furthermore, the trophoblastic villi, which differentiate in the trabeculæ of the I.V.S., do not possess a blood circulation until the embryonic heart commences to beat at about the twentieth day after fertilization. By this time, however, the embedded chorionic vesicle is approximately spherical in shape and possesses a diameter of about 7 mm. Up to this stage, therefore, and as a consequence of the absence of an embryonic circulation, no direct means exists for the transport of required metabolites to the embryo, across what are, from the sixteenth day onwards, quite considerable distances. Diffusion and, possibly, a slow circulation of the fluids in the intrachorionic, extra-embryonic spaces must be sufficient to meet the requirements of growth and differentiation. Certainly no "placental membrane" in the usual sense of this term, and which I shall be considering later, yet exists. Nevertheless, the embryo and its membranes grow and the chorionic vesicle takes up fluid and expands.

The I.V.S. during this period remains very small. As it is supplied chiefly by venous blood the hydrostatic pressure in it cannot but be very low. Two problems, therefore, are presented by the situation. Firstly, how does the trophoblast take up the required metabolites? And, secondly, how, in fact, are these substances transferred to the embryo?

An attempt to answer the first of these questions involves a brief consideration of the cytoplasmic surface presented to the maternal organism by the conceptus. Immediately after implantation this surface is syncytial in nature and over large areas of the maternal-fœtal boundary it will remain in this condition throughout gestation. In some regions, however, the boundary syncytium becomes differentiated into, or is replaced by, cytotrophoblast. The early syncytium is clearly destructive to maternal endometrial tissue, and the presence in it of phagocytosed red blood cells and other debris shows that it can engulf particulate matter. The question, therefore, essentially is:—How does the syncytium take up particles such as these which are large enough to be readily seen with light microscopy? Unfortunately, electron microscopy has not yet been exploited in the study of the trophoblast in very young stages of human implantation. By comparison with observations (Boyd and Hughes, 1954) on the fine structure of the chorionic villus in older human placental specimens, however, it can be suggested that the early trophoblastic cytoplasm possesses an apparatus which enables small droplets of fluid to be taken up (pinocytosis) and particles of greater than molecular size, such as red blood cells or cytoplasmic debris, to be engulfed (phagocytosis). On extensive parts of the surface of the chorionic villi of later stages and of the early syncytium lining the I.V.S. a so-called 'brush border' can constantly be seen with light microscopy. When ultra-thin sections of this brush border are examined with the electron microscope it is found to consist of myriads of microvilli which may, individually, be as much as 2 μ in length. We recorded the presence of numerous vacuoles in the syncytial cytoplasm underlying the microvilli, and suggested that, in the human placenta, the microvilli were wafting fluid into the cytoplasm. Such pinocytosis had, in fact, been suggested earlier by Wislocki and Bennett (1943) from their observations based on light microscopy. Later E.M. studies on the human placenta by Wislocki and Dempsey (1955) and by Sawasaki, *et al.* (1957), have supported such an interpretation for the brush border. By analogy the presence of the brush border in the early implantation stages leads to the conclusion that when the trophoblast of such stages comes to be investigated with the E.M. it will be found to possess microvilli such as are present on the syncytial covering of the chorionic villi of an embryo of as early as the 6 mm. C.R. length stage. I suggest, therefore, that from the earliest stages of placental development, the syncytium does not behave merely as a semi-permeable membrane. Through the possession of a brush border, constituted by the microvilli, the engulfing of substances in the form of particles even larger than the largest macro-molecules is possible.

This suggestion can be supported by other observations. In the first place there is histochemical evidence. It has already been stated that the uterine glands produce a copious secretion and that through the cytolytic activity of the

trophoblast this secretion can come into intimate relation with the syncytium. One of the products of secretion is glycogen which can be readily identified histo-chemically. In implantation sites of somite embryos (Boyd, 1957) glycogen can be identified in large amounts in the decidua, in the cells of the uterine glands, and in the glandular lumina. It is also present in the cytotrophoblast, in cytotrophoblastic spaces, in peripheral bays of the I.V.S., and in areas of the syncytial covering of the villi orientated towards the endometrium (Pl. III, Figs. 9 and 10). In this last site the glycogen can be seen at all levels between the surface, facing the I.V.S., and the deeper part of the syncytium, where it is particularly heavily concentrated. Small glycogen particles can be seen to have been caught up in the brush border and the appearances suggest strongly that they are being phagocytosed by the syncytial surface. Equivalent appearances have also been described recently by McKay, *et al.* (1958), in a report on the distribution of glycogen in the syncytium of early human implantations. Observations on the behaviour of pigment granules found in the cells of, and presumably produced by, some of the uterine glands also point to the conclusion that there is active syncytial phagocytosis. These granules can be found not only in gland cells (Pl. III, Figs. 11 and 12); they are also present in the adjacent cytotrophoblast (Pl. III, Fig. 13), in the brush border, and in the general syncytial cytoplasm of related villi (Pl. III, Fig. 14).

Observations such as these on the human placenta, and much experimental work on mammals with very different placental structure (Brambell, *et al.*, 1951); Brambell, 1959; Wislocki, 1955; Dempsey, 1958) indicate that the placenta cannot be regarded as a simple semi-permeable membrane, permitting only of passive diffusion. Active transport mechanisms are also at work. There will, of course, be differences between the transfer of macro-molecules (and, as I have suggested, even of particulate matter) on the one hand, and of electrolytes and gases on the other. But it seems most likely that for the passage of all substances across the placental barrier cytoplasmic activity is involved. According to the nature of the substances transferred, the placental type, the actual region of the placenta, and its age, this transference involves, to differing degrees, such mechanisms as enzymes, "carrier" molecules, phagocytosis and pinocytosis. Grosser, who made considerable contributions to our knowledge of human and comparative placental morphology (summarised in 1927), based his well-known and widely accepted classification of the placenta on the degree of intimacy of fusion of the fœtal and maternal tissues. His terms epithelio-chorial, syndesmo-chorial, endothelio-chorial and hæmo-chorial, arranged in this order, give a striking summary of the diminution in the width of the tissues separating the maternal and fœtal bloods in different mammalian types. As Wislocki (1954) and others have shown, however, the gradual reduction in width of the thinnest placental regions is not nearly as dramatic as Grosser's classification suggests. In my opinion it is now quite clear that deductions relating to placental transfer and to relative placental efficiency from Grosser's classification are not well founded. Indeed such deductions can be very misleading.

The suggestion that there can be an active uptake of macromolecules by the

placental membrane is supported by our knowledge on the transfer of homologous antibodies from mother to fœtus. Indeed, plasma proteins in general appear to be able to transgress the barrier (Schechtman, 1957). The amounts of such proteins transferred may only be in trace quantities and devoid of metabolic significance. But that macromolecules can get across at all is the important and impressive fact. It is, however, possible that, once transferred, and through enzymatic breakdown, they contribute smaller molecules which can be used in embryonic synthesis. If the foreign protein macromolecules, even when they are only transferred in trace amounts, are not broken down special problems arise in relation to the antibody system of the fœtus, which, as is now well known, does not become operative until relatively late in development. Moreover, it is conceivable that the addition of macromolecules of specific pattern to the orientated molecular population of the embryo could have profound morphogenetic significances (Weiss, 1950).

Apart from the transference of macromolecules in trace amounts, however, there remains the possibility that some substances are being transferred in quantities sufficient to have metabolic importance and to serve as sources of energy or of structural material for the embryo. The great significance of glycogen, in this regard, will be obvious for the advantages of the ready availability of this polysaccharide to a system which is as relatively anærobic as the early implanted ovum would appear to be needs no stressing. What happens to the glycogen when it transgresses the syncytial surface is, of course, part of the second of the two questions I asked in an earlier paragraph. Some of it, at least, is probably broken down and utilised in the syncytium itself. Some of it may pass as glucose into the embryonic fluids and thence to the embryo. There is even the possibility that, in the early stages, some of the glycogen may be transferred as such to the embryo. A fact which, I think, is of particular significance is that the availability of glycogen in large amounts is largely restricted to the early stages of human placentation. With disappearance of the basal decidua, and of the associated uterine glands, glycogen diminishes in the villi and disappears from the syncytium. When it is remembered that a free circulation in the I.V.S. is established late, so that the early conceptus is under conditions of distinct anærobiosis, the particular association of glycogen with early development is, perhaps, not surprising.

In the latter stages of development, however, it is the maternal circulation in the I.V.S. which is of paramount importance in the supply of oxygen, electrolytes, and the basic nutritive substances to the growing fœtus. Nevertheless, our knowledge of the mechanism of this circulation is still meagre. The generally accepted view in the first three decades of this century stemmed from Bumm (1893), who considered that the endometrial spiral arteries opened on the placental septa well away from the basal plate and that the uterine veins opened about the middle of the uterine surfaces on the maternal cotyledons. By this arrangement he considered that the circulation of the blood through the I.V.S. was explained. His conclusions, it should be noted, were based on the histological study of delivered placentæ. Much more recently Spanner (1935, 1936) restudied the

anatomical arrangements by the injection techniques and concluded that Bumm's explanation was unacceptable. Spanner described the endometrial arteries as opening into the I.V.S. through the basal plate itself, and not on the placental septa. Furthermore, he considered that the maternal blood, on reaching the I.V.S., was guided by the septa towards the chorionic plate, whence it was *all* drained to the periphery of the placenta. Spanner described, in this situation, the constant presence of a dilated portion of the I.V.S. which he called the "marginal sinus." In his opinion it was only at the placental margin, and by way of this sinus, that communication was established with the uterine veins. Thus he readily explained the circulation in the I.V.S. and his interpretation was widely accepted. In particular his concept of a marginal sinus has been eagerly seized upon, especially by the clinicians, for it has been considered to provide an adequate and satisfying explanation for certain hæmorrhagic catastrophes of pregnancy. A number of investigators, however, including Hamilton and Boyd (1951) have not been able to confirm all of Spanner's findings, and consequently cannot accept his interpretation of the circulation in the I.V.S. Hamilton and I have based our study on a large number of *in situ* placentæ available in extensive serial section. We have found the openings of the endometrial arteries, into the I.V.S. of the mature placenta, to be distributed at intervals over the whole of the basal plate. I, myself (1955), have, by computation, estimated that at the fourth month of gestation there are between 100 and 150 such arterial openings; at term the number varies between 180 and 320. Spanner considered that there were about 500 such arterial communications with the I.V.S. When it comes to the veins draining from the I.V.S., however, the situation is quite different from that envisaged by Spanner. Thus a marginal sinus of the I.V.S. is not constantly present (Pl. IV). Moreover, venous openings from the I.V.S. are to be found regularly, and freely, over the whole of the surface of the basal plate. This surface, of course, includes the placental edge; it is, therefore, not surprising

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**PLATE I, Fig. 1.** Human embryo (H.789) of 33 mm. C.R. length in its chorionic sac, to show the implantation site and general relationships of the developing placenta. (X 1.25).

**Plate I, Fig. 2.** Chorionic sac and developing placenta of the same specimen shown in Fig. 1 after removal of the embryo. The cut umbilical cord is attached to the chorionic plate of the placenta. The basal placental plate appears as a whitish line across the greater part of the implantation area. This line separates the chorionic villi and I.V.S. from the basal decidua. The decidua capsularis (reflexa) shows an extension of villi and I.V.S. in relation to its lower half. The upper part of the capsularis, however, together with the abembryonic portion of the chorion, is markedly attenuated. In this region, consequently, the interior of the chorionic sac is separated from the uterine lumen by only a very thin double layer of maternal and fœtal tissue. The decidua parietalis (vera) can be seen on either side of the placenta, extending up to the cut margin of the uterus. (X 1.25).

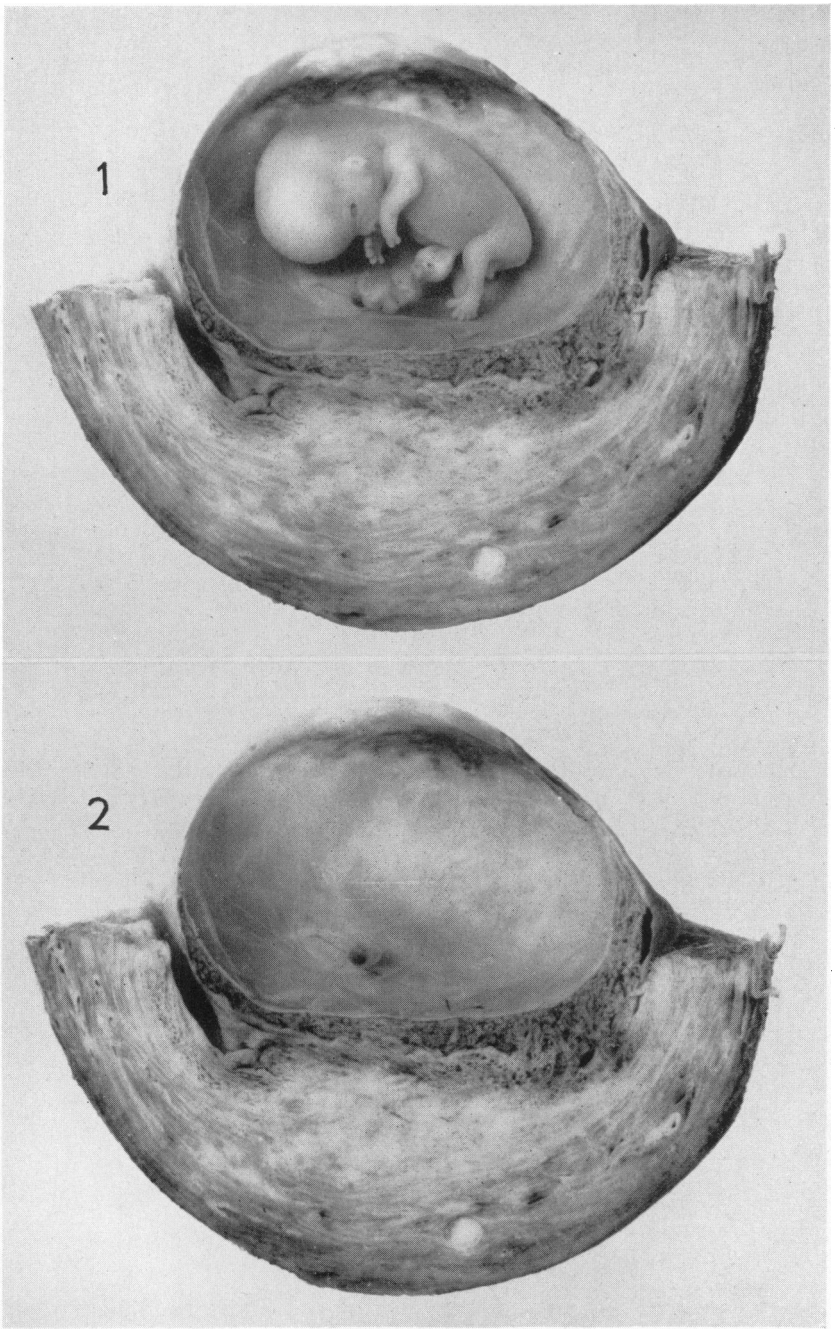


**PLATE I**

**PLATE II, Fig. 3.** Two clumps of syncytial cells in the myometrium of a uterus from a 157 mm. C.R. length human pregnancy (H.219). There is no sign of any cellular reaction to the presence of these masses of syncytium which are interpreted here as being of fœtal origin. (X 110).

**Plate II, Fig. 4.** High power view of one of the masses of multinucleated cytoplasm shown in Fig. 3. (X 480).

**Plate II, Fig. 5.** Two syncytial sprouts in a uterine vein well removed from the region of placental attachment in the 157 mm. specimen (H.219). (X 140).

**Plate II, Figs. 6 and 7.** Higher power views of the syncytial sprouts shown in Fig. 5. Such sprouts pass in the mother's venous blood to her lungs. They possess diameter of up to 70 microns. (X 480).

**Plate II, Fig. 8.** Section of portion of implantation site in a 28 somite (26-day) human embryo (H.710) to show a (V-shaped) space in the cytotrophoblast. This space contains glandular secretion and cellular debris together with a syncytial sprout. Two necrotic glands are present in the photo-micrograph. The peripheral part of the I.V.S. is shown above, surrounding the chorionic villi.

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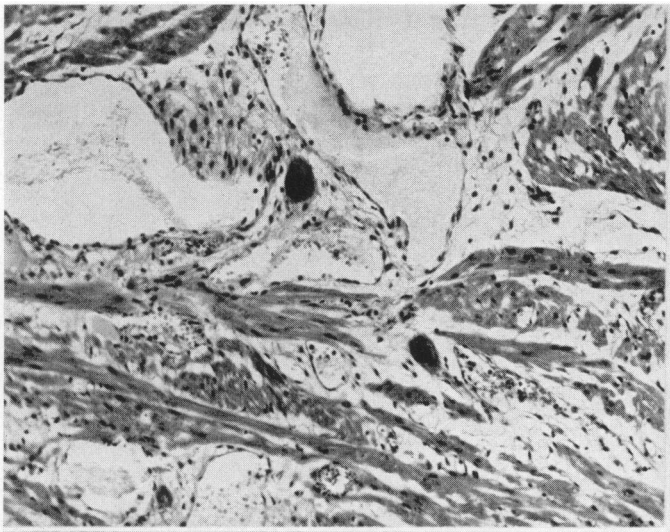

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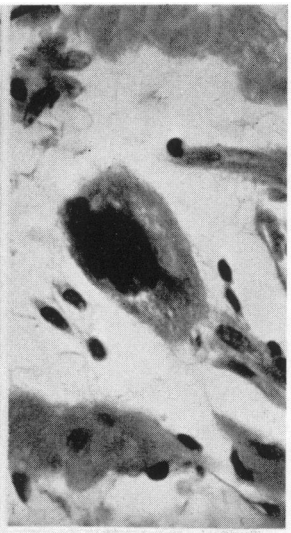

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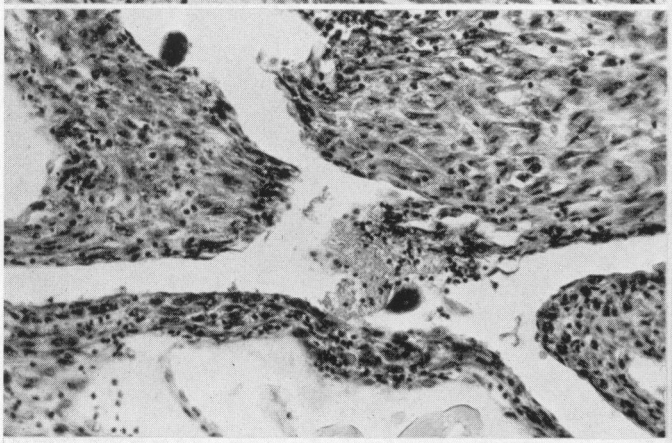

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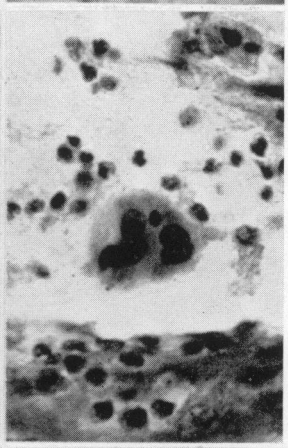

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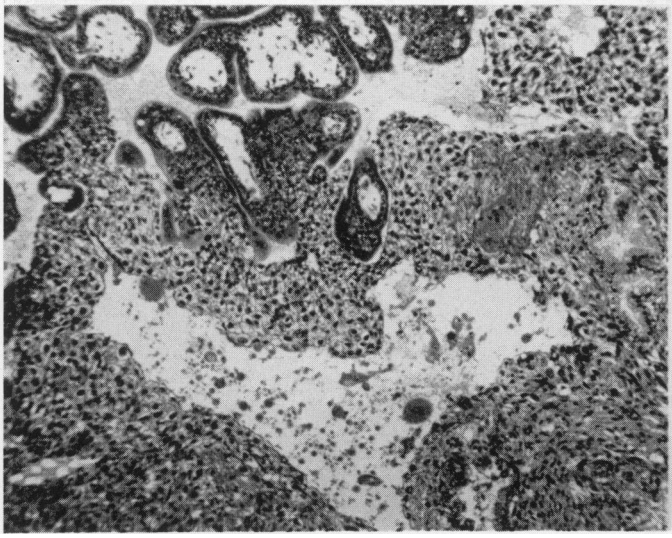

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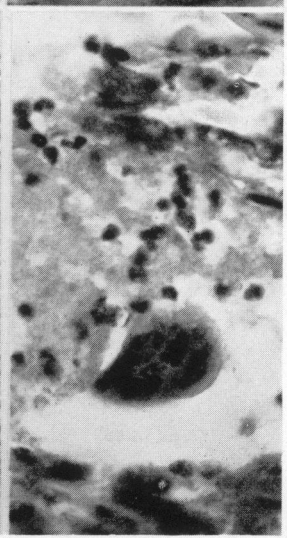

**PLATE II**

**PLATE III, Fig. 9.** Section of margin of chorionic villus from a somite human embryo to show distribution of glycogen which is darkly stained by the P.A.S. technique. Note the heavy concentration of glycogen in the syncytium which is in contact with the I.V.S. (X 535).

**Plate III, Fig. 10.** Section of margin of chorionic villus from a somite human embryo, stained with the P.A.S. technique. Note heavy concentration of glycogen in the syncytium on the right side of this photo-micrograph. Small glycogen particles can also be seen in the brush border bounding the I.V.S., which is situated above. (X 840).

**Plate III, Fig. 11.** Section of basal decidual gland in a somite human implantation site to show distribution of pigment granules. (X 125).

**Plate III, Fig. 12.** Higher power view of part of wall of gland shown in Fig. 11. (X 610).

**Plate III, Fig. 13.** Pigment granules in cytotrophoblast of somite human embryo. This cytotrophoblast is situated adjacent to the gland shown in Figs. 11 and 12. (X 610).

**Plate III, Fig. 14.** Pigment granules in syncytiotrophoblast adjacent to the gland shown in Figs. 11 and 12. (X 610).

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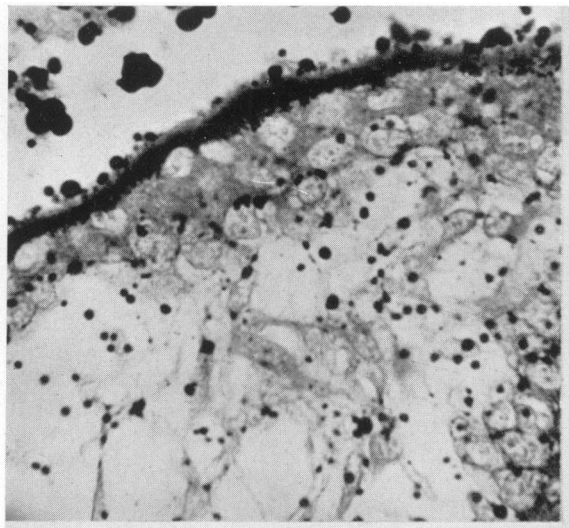

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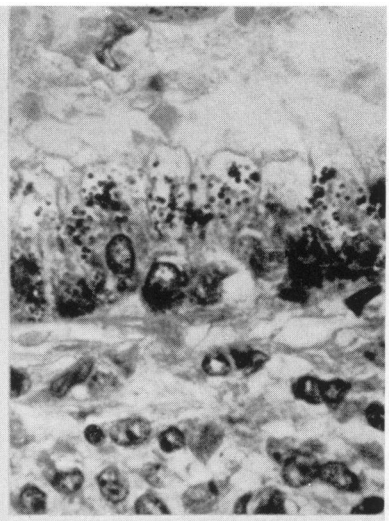

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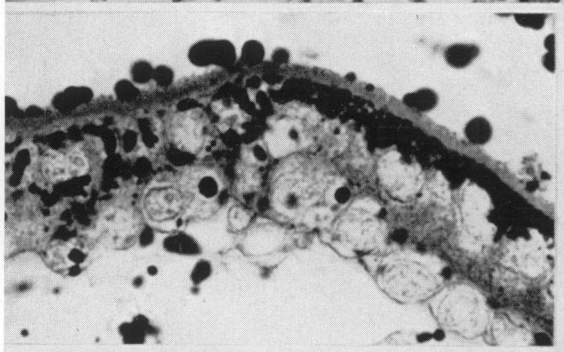

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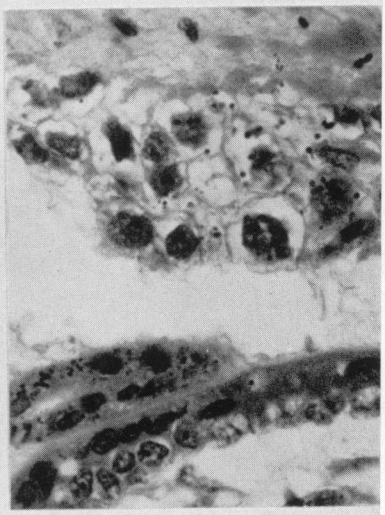

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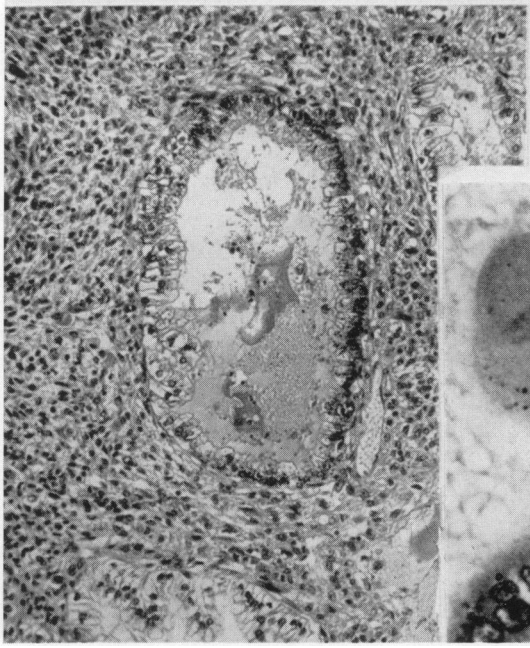

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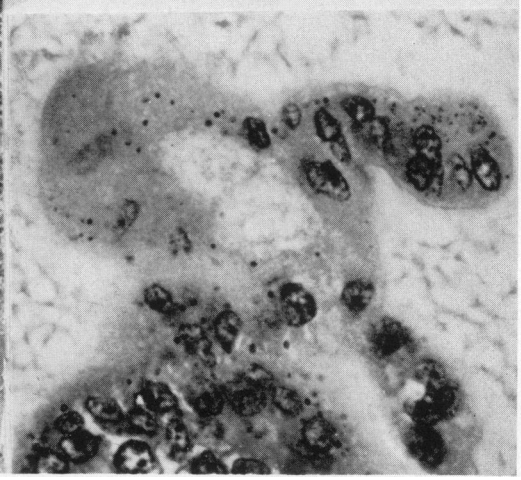
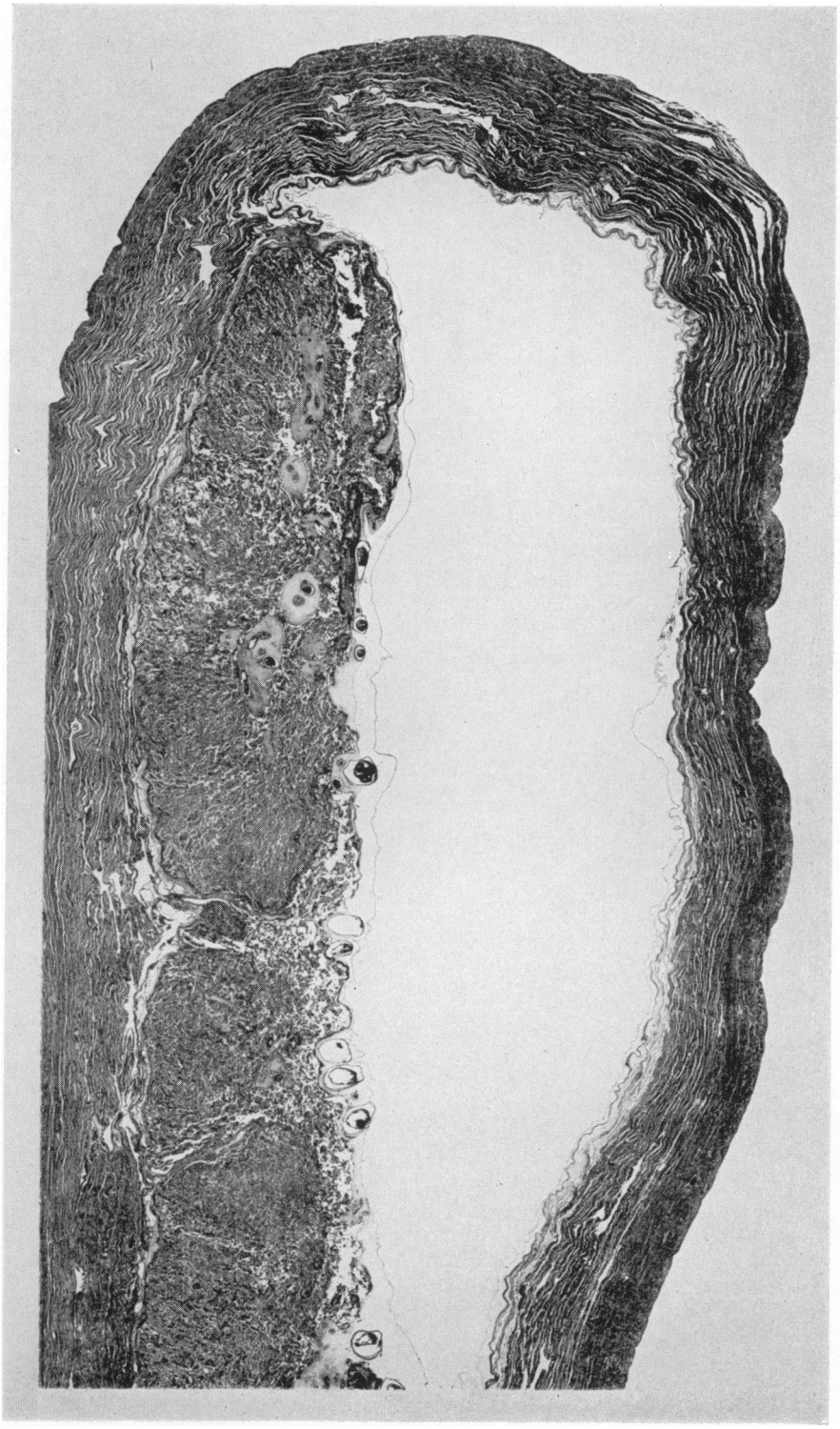


**PLATE III**

**PLATE IV, Fig. 15.** Section of an *in situ* placenta from a 260 mm. C.R. length human pregnancy. Note absence of marginal sinus and uterine venous plexus related to central part of basal plate. By this stage the whole of the uterine lumen has been obliterated and the decidua reflexa has fused with the decidua parietalis. The amnion can be seen as a fine membrane lining the whole of the chorionic cavity. The density of the villi in the I.V.S. is, in general, uniform, but there is some appearance of a sub-chorial lake in relation to the central part of the chorionic plate. (X 2.5).



15.

**PLATE IV**

that, from time to time, communications can actually be found passing from the marginal portion of the I.V.S. to the decidual veins. Hamilton and I are convinced, however, that there is free drainage of the I.V.S. into veins that communicate with it over the whole basal surface of the placenta. Finally, we follow Stieve (1942) in considering that the arrangement and nature of the placental septa is such that these curious, and ill-understood, partitions cannot serve the function allocated to them by Spanner.

The I.V.S. is, of course, an enormous and complicated arterio-venous anastomosis. With the arrangement of its afferent arteries and efferent veins, such as I have described, the problem arises as to how, in fact, the arterial blood entering the space from the spiral vessels is prevented from being short-circuited into the orifices of the contiguous veins on the basal plate. Dr. Elizabeth Ramsey (1955) has suggested, for the macaque monkey placenta, that the head of pressure in the endometrial arterial orifices is sufficient to drive the blood towards the chorion and that thus, and without the need of the septa to act as baffles, or "dividers," short-circuiting is avoided. Her suggestion has been supported by Borell's (1958) studies on the human placenta, using arterioradiographic techniques. In my opinion, however, we do not yet know sufficient about the I.V.S. itself, or about the pressure conditions in it to be able to accept with complete assurance Dr. Ramsey's interpretation. There may, for example, be preferential pathways in the I.V.S. The existence of such pathways could, indeed, explain certain features in placental infarction. The Braxton-Hick's contractions of the myometrium may also come into the explanation. Furthermore, there are extraordinary alterations in the arterial structure which, as they seem capable of influencing the pressure conditions, must be taken into account in explaining the I.V.S. circulation.

This last statement leads to a, necessarily brief, consideration of these coiling, or spiral, endometrial arteries. Discovered in the early eighteenth century and described in some detail by William Hunter in the classical account of the decidua in his *Anatomy of the Gravid Uterus*, these arteries undergo marked changes in the course of the non-pregnant uterine cycle. During pregnancy the alterations in the vessels are even more remarkable (Boyd, 1955). They are tapped by trophoblastic erosion relatively late in implantation and they then soon show several remarkable alterations. In the first place, and at an early stage of development, their walls in the near vicinity of the placenta show a striking degenerative appearance, involving hyaline necrosis and disappearance of the muscle cells in the *media* of the vessels. If a single spiral artery is followed from the myometrium to its termination in the I.V.S. one segment of it is often found to be very much narrowed before the region of terminal dilatation, near its orifice, is reached. If this narrowing and the spiral nature of the vessels are together taken into consideration it can be concluded that, in life, the blood pressure in the arteries is very much reduced along the length of their course. Finally, however, and perhaps most remarkable of all the arterial modifications, many of the spiral vessels come to contain within their lumina cells of uncertain nature. Some of these intra-arterial cells are certainly of fœtal origin, being

derived from the cytotrophoblastic shell. Some, however, may be of maternal origin, for they could be derived from the arterial endothelium or even from the decidua. Such cells, whatever their origin, are found in many of the spiral arteries, and often at quite considerable distances from the basal plate, until as late as the sixth month of gestation. None of us has any adequate notion as to their precise significance. Their presence in the vascular lumen must, however, add to the general cutting down of the blood pressure in the spiral arteries which contain them. In many vessels, indeed, these cells are so numerous, and become so crowded, that blood-flow in these arteries must be reduced to near, or even complete, cessation.

Such aggregations of cells are only found in the spiral arteries—they are never seen in the veins opening out of the I.V.S. The veins themselves are thin-walled and show none of the alterations that might be expected if arterial pressure was being transmitted to them. Not infrequently, however, other plugs, formed by the tips of adjacent chorionic villi, are found to extend into the veins. Such "herniation" of villi into the venous orifices may only be a post-mortem effect and due to contraction of the uterine muscle. Whether this is so, or not, the herniated villi can readily be identified in sections of *in situ* placentæ, a fact that is most useful in identifying the venous orifices from the I.V.S.

Finally, I come to the intervillous space itself. To deal with it adequately would require at least a whole lecture, and such an attention to anatomical and histological *minutiæ* that your attention might well not be held. In summary, however, I can say that the space is very extensive and that, both in shape and in capacity, it probably fluctuates widely during life. It is lined almost, but not quite, entirely by syncytio-trophoblast and, as has been described earlier, this syncytium shows a brush border constituted by myriads of microvilli. It is through the syncytium that the maternal-fœtal exchanges, in both directions, take place. Whether these exchanges are active, as the evidence strongly suggests, or passive, the total area of the syncytium will be one important factor in determining the amount of the transference of substances. Estimations by different investigators of the total area available for exchange, which, in effect, means the total villous surface, vary from four to fourteen square metres for the mature placenta, with the consensus of opinion inclining towards the larger estimation. Even allowing for possible errors in estimation and considerable variations from placenta to placenta, the total area for exchange is certainly a very large one. It corresponds closely, as Wilkin and Bursztein (1958) have pointed out, to the total absorptive surface area of the intestinal tract of adult man. And the area must provide a considerable safety factor in placental function. The deposition of fibrinoid and of fibrin itself in the I.V.S. commences early in development and by the time of placental maturity is often very extensive indeed. The presence of these deposits on the villi must cut down considerably the efficiency of the syncytial membrane. Often, also, there is extensive formation of thrombi in the placenta. I have seen late placentæ in which anything from one-third to one-half of their substance must have been rendered functionally ineffective by such quasi-pathological changes. And yet these placentæ had been

efficient enough to provide adequately for the growth and differentiation of their dependent fœtuses, for these were of size and weight proportionate to their developmental ages. The existence of this very high margin of "placental reserve" is not the least of the many puzzling features of the maternal-fœtal relationship. Like the length of so many umbilical cords, the functional capacity of the placenta is, in relation to the exchange problem, much in excess of what is normally required of it. This excess may be due to some, possibly temporary, wide mesh in the sieve of natural selection. It may, however, have some quite different explanation. Thus the placental tissues produce important hormones, and the final size of the organ may be related to this aspect of its function rather than to the part it plays in the two-way traffic in metabolites.

In the time at my disposal I have only been able to draw attention to a few facets on the rough unhewn rock that constitutes the unopened core of the placental problem. The organ has not received anything like the attention its importance demands, and will, I feel sure, increasingly receive. It did not even receive a name until 1558 when Realdo Columbus, in his *De re anatomica*, first used the term placenta. Four hundred years, you may think, is not a short time in the history of science. In fact, however, it has effectively been only the last hundred years that has given us our present-day knowledge of the placenta. And the number of those who have worked on it is so small that I could readily list most of them for you. We can look forward, I believe, to a continuing expansion of interest in placental morphology and function.

And, surely, the placenta will deserve this increasing attention, for it is the essential structural basis of the prenatal relationship between mother and child. Devoid of a direct nerve supply, it integrates itself into the *milieu intèrne* of two organisms. Derived by differentiation from cells that possess the potentiality of living for seventy, or more, years, its constituents sacrifice themselves after ten lunar months. Built up of disparate cytological elements derived from two heterozygous individuals, it has functions so diverse as to overlap those carried out, in the adult, by lungs, liver, intestinal tract, kidneys, and endocrine glands. Wordsworth certainly did not have the placenta in mind when he wrote:—

> "there is a dark
> Inscrutable workmanship that reconciles
> Discordant elements, makes them cling together
> In one society."

Nevertheless, the quotation, in the present context, is apt. For any satisfying explanation of the relation of the unborn child to its mother the darkness of the intra-uterine workmanship must first be made visible and the inscrutability replaced by biological answers to rational questions. In the course of satisfying our curiosity on the placenta there can, in my opinion, be no doubt that obstetrics and pediatrics will be forwarded. It is because I strongly hold this opinion that I have dared to present a non-clinical subject in an oration that has as its prime purpose the perpetuation of the memory of a distinguished clinician.

## References.


Borell, U. (1958). *Geb. u. Frauenh.*, **18**, 1.

Boyd, J. D. (1955). *Trans. Macy Foundation on Gestation*, **2**, 132.

———— (1957). *Proc. Anat. Soc., J. Anat., Lond.*, **91**, 595.

Boyd, J. D., and Hamilton, W. J. (1952). Cleavage, development and early implantation of the egg. *Marshall's Physiology of Reproduction*, **2**, Third Edition, edited by A. S. Parkes.

Boyd, J. D., and Hughes, A. F. W. (1954). *J. Anat., Lond.*, **88**, 356.

Brambell, W. F. Rogers (1959). *Biol. Rev.*, **33**, 488.

Brambell, W. F. Rogers, Hemming, W. A., and Henderson, M. (1951). *Antibodies and Embryos.* Athlone Press, London.

Bumm, E. (1893). *Arch. f. Gynäk.*, **43**, 181.

Dempsey, E. W. (1958). *3rd Sci. Conf.*, Assoc. Aid Crippled Children, 1.

Grosser, O. (1927). *Frühentwicklung, Eihautbildung und Placentation.* Bergmann, Munich.

Hamilton, W. J., and Boyd, J. D. (1951). *Proc. Roy. Soc. Med.*, **44**, 489.

Hertig, A. T., and Rock, J. (1956). *Am. J. Anat.*, **98**, 435.

McKay, D. G., Hertig, A. T., Adams, E. C., and Richardson, M. V. (1958). *Obst. Gynec.*, **12**, 1.

Medawar, P. B. (1958). *Proc. roy. Soc., B.*, **149**, 145

Park, W. W. (1958). *J. Path. Bact.*, **75**, 257.

Ramsey, Elizabeth (1955). *Trans. Macy Foundation on Gestation*, **2**, 229.

Sawasaki, C., Mori, T., Inove, T., and Shinmi, K. (1957). *Endocrinol. Japon*, **4**, 1.

Schechtman, A. M. (1957). *Internat. Rev. Cytol.*, **5**, 303.

Spanner, R. (1935). *Ztschr. f. Anat. u. Entwicklungsgesch.*, **105**, 163.

———— (1936). *Ztschr. f. Anat. u. Entwicklungsgesch.*, **106**, 350.

Schmorl, G. (1893). *Pathologisch-anatomische Untersuchungen über Puerperal-Eklampsie.* Leipzig: Vogel.

Stieve, H. (1942). In *Biologie und Pathologie des Weibes.* Bd. 7, Second Edition. Edited by L. Seitz and A. I. Amreich. Urban and Schwarzenberg, Berlin.

Weiss, P. (1950). *Quart. Rev. Biol.*, **25**, 177.

Wilkin, P., and Bursztein, M. (1958). *In Le placenta humain.* Edited by J. Snoeck. Masson, Paris.

Wislocki, G. B. (1954). *Trans. Macy Foundation on Gestation*, **1**, 176.

———— (1955). *Trans. Macy Foundation on Gestation*, **2**, 181.

Wislocki, G. B., and Bennett, H. S. (1943). *Am. J. Anat.*, **73**, 335.

Wislocki, G. B., and Dempsey, E. W. (1955). *Anat. Rec.*, **123**, 133.

Woodruff, M. F. A. (1958). *Proc. roy. Soc. B.*, **148**, 68.